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		Olu	Lys	Ala	Phe	Ser		020	Val	110	Pro 176	Start	She	Ser	212	175	
	5	ŭ1 v	giy	Ala	Thr	900	Sin	Asp		Ran 185		Mes	Siens	Asa	31e 380	Val	63
11	G	Sly	Mis	ule 163		Ala	Pinc	üla	Mat 200	Leess	Lys	Sep	Tier	fle		61s	01:
1:	5		Sla Slo	Glu	Trp	Asp	Arg	Dec 235		Pro	Val	Gla	Ala 220		Fro	ile.	Pr
21		225	diy	(I) n	Ile	Arg	01u 250		Ang	Sly	Ser	Asp 235	Ile	Ala	Gly	Spek	7h.
		Se I	Thr	Pric	ill a	00 u 245	Gin	Leu	61a	тер	Mer. 288		GIY	Asst	aro	PE0 288	ΥI
2		Pro	Vas	ΟLY	Asn 265	236	TYX	Lys	Arg	Trp 265	The	Tle	Lavu	oly	Led	Asz	ly
36	0	Lie	VA.	A29 276	Mer	Tyr	श्वतः	Pre	783 283	Ser	Ile	Sev	Asp	110	Lys	Sia	001
3!	5	Pro	lys 290	G) s	F20	Phe	Arg	Asp 20%		Val	Asp	Asy	She 300	Phe	Lys	8.)a	Le
40		Arq 30s	Alw	ain	Ø1n	Axa	2967 300	din	Aug	fav	lys	319 318	Typ	Nec	Thr	Oyu	32
		les	Les	VA)	d'in	5.60 3.03		Aen	Pro	890	Cys 33a	1.78	80 r	114	Léu	Lys 139	
43		i e :	639	505	915 340	sis.	Thr	Less	đầu	61 u 345	Met	Met	inc	à là	Cys 350	dia	(31)
54	0	Val		Siy	980	Sty	His	Lys	A) & 360		va i	Leu		GIG		860:	80
5	5	din	Ala 375	Gla	Gla	The	Asc	Tie 375	Mer c.	Most:	Glu	Ang	dly	ken	Phs	824	cri
64		Gla 385		Arg	Ile	Lys	Cys		Assi	Cys	div	195	Gle	ÇIY	His	Lev	A1.
		Arg	Apri	CA8	Arg	Ala 405	Pro	Arg	iye	1578	Giy alo	CVS	Tep	Lys	Cys	617 617	Sy.
6		atu	Oly	His	Gin 420		tys	Asp	Cys	752 425	glo	Arg	SIA	Ala	Adn 43c	23/2	(Jan)

	373	Lys	110	Top	Pro	Ser	Sex	646	#33	25.00	PAR	GLY	443	2956	Pro	124
-5	Sea	8.rs 480	Pre	GLu	PTG	The	838 656		Pxc	83.3		b#4 €60	Phe	oly	Met	61;
10	0)% 465		;le	Ala		\$400 470		Lyw	Gla	alu	Gln 478		Asp	Arg		48
15	Val	Pro	Pro	Leu	Val.		Leu	Sye	Sec	Let 490		GIY	Asn	Asp	970 495	
20	Sec	Oln	oth	500 500		Tie	Bor	210	11e 909	Gi u	THE	¥a)	Fro	Vol. 510		200
	Lya	P250	61y 515	Mer.	Amp	817	Pre	Lys 530	863	Lys	Gip	Trp	Pro 925	Less	The	27
25	g)u	Lys 530	lle	ley a	Ala	Len	Tar 939	Glu	lle	Суч	The	01a 540	Met	di a	Lys	gk
30	41y 545		Flee	Shr	Lyn	Tie 550		Prop	Cha	Ann	910 \$\$\$		Asn	The	Pro	85
36	Phe	Ala	11.0	Lys	Lys	Lys	800	Ser	The	148 570	Tip	Aug	296		Val 878	
40	Pho	Asp	Wise	1.60 380	Ass	Lyna	ary	Thr	01n 365	ARP	Phe	Trys	als	V23 590	Gèn	Det
	aly		\$250 \$95		Pro	Ala	Gly	1/6ts 6 0/0	Lyn	byo	Lys	Lys	84K 605	V42	Thu	50
45	Len	A99 610	Val	GLY	Asp	Als	TYF 615	Pne	997	783		ten 620	Anp	Glu	Asn	Phy
50	A119 625		Tyr	The		Pns 636		ile	FXC	ser	TDE 635		Astr	Glu	Thi	841
55	diy	Val	Ary		Cha 645		Asm	Val		PY0 683		oly	Trp		01y 653	
60	Pro	Ala	Tie	Phe 360		Sex	Ser	Met	7hr 865		116	Zen		880 670		Alt
	967		A80 675		Oliu	lle		Tie 830		91a	ĭyk		A16		Les	27.
65	76)	GRy 690	Ser	Asp	imu	oft a	11e	Gly	GIn	Ris	Arg	7hr	Lys	Пg	(d) u	Gi

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	Leu 765	arg	Ala	Eis	Leu	Less 716	Ser	Trp	агу	Phe	The	The	Pro	Asp	Sye	Dy:
5	Sis	ale	Lys	Glw	Pre 725	Pro	she	Leu	Trp	Med.		Tyr	Olis	leru	#ia 735	
10	Asp	tys	Tro	The 740	VAL	GD ve	Pro	T) n	9et. 765	Len	Pro	Asp	byn	01 u	Ser	Tre
15	Thr	yaı.	\$20 766	Lep	318	g) e.) NE	280		G) y	tys	tieu	A#5 766		Ala	San
20	Gl n	110	žyr.	Ain.	91 y	lle	Lys 775	Val	Lyn	Gla	Leo	Cys 783	Arg	Sites to	beso	λr
	91y 788	Ala	sys	Ala	1490	769	Asp	124	Val	Thy	7.60 7.95	The	(G) la	630	A) s	800
25	Leu	Glu	Leu	Ala	81c	Asn	λrg	dlu	tle	beu 810		Asp	Pro	ve1	sis ers	(F)
30	¥a2	Tya	2)x	Aug: 820	SES	Ser	Lys	Asp	Less 925	Val	ala	Shu	ile	03%	Lys	Gla
35	gly	913	805		Trp	Thr	TYX	@ls 8x0	lle	Tyr	Gla	Glu	9x0 883		Lys	Aas
40	les	Ly3 850		oly	lys	1yx	A15 885		Lys	Arg	862	814		The	Ass	Aug
	Val ess	äng	Ole	Lette	X.1 a	01u 870	Val	9al	din	tigs	981 875	Aia	566 t.	GIR		886
45	V.S.Z	718	Trp	Siy	14s 805	The	Pro	tys		5.95	Les	51.0	lie	Gin	1.yx 535	
50	The	120	di.	The 960	2rp	Trp	Met	Aug	Tyr	Trp	Oln	ā)a	The	Trp 910	Die	Pge
55	40 t	Tep	G1-0 93-9	Phy	Va1	Asn	The	Aro 920	Pro	Lets	Vsl	Lys	Leu 925	Ťry.	tyr	(i) i
60	Less	61u 830	Lys	Asp	Prh	lie	Lau 93%	aly	Ala	93%	The	5he 940	Tyr	Val	Asp	diy
	Alx 545	Alu	Asr.	ytá	03 a	Thr	Lyn	[Mil	sty	Lyx	A33 986	diy	Ту≭	Vni	The	Asg 966
65	Arg	Gly	Ass	G) B	678 685	Wal	Val	Sex	Leu	The 970	Sla	The	The	Sec	G1:15	1.78

	Thr	320	lew	Bis 560	Als	110	Les I	John A	1s I 85	64 G	A RE	ap še	x /31 59	y 3e	r-Olu
5															
	Val	Asn	118	Val	Thr	Asp	Ser (003 003	Tyr	A.s	3,4932	gra 1	2e 003	130	Oln Ala
10	Gla	2101	Ang	Arg	Sex	- Olo	59x 1013	044	l.eu	Val	240	Glu 1920	Tie	118	919
15	Lys	1626	tie	gty	t.ys	A SQ	tys	1 ta	ryr	-5.40%	Ser	77p 1035	vai	Pro	Alz
20	Nie	Lys 1045	91y	Ile	Gig	Gly	Asn 1048	Giu	Gla	861	Asy	lys 1950	iou	Val	Ser
	ERT	1699 1699	174	Arg	Lys	Val.	1000	992-3	Leve	Assp	Giy	114	Asp	Lys	Kla
25	Ole	01u		37.8	- Glu		Tyr		Ser	Ass	Trp	A29		Mei	Ala
30	Ser	A89 1088		Agr		Pro	PY0 1090	lie	Va.3	818	Lys	40 v 1898	Lle	78.7	Aix
35	Ser	Cys 1100	Asp	Ly S	Cys	din	1.00	Lys	Gly	Glu	A1.6	Met 1115	His	Gly	Win.
40	Val	Asp 1115	Cys	SAY	PEC	y i.b	110	typ	G1a	bén	6.3 a	Cyre 112%	Tha	Mis	Lev
	838	(3) y 1135	T.y.w	70)	314	Len	98) 1138	Ala	V.X.	81.8	983	Ala 9340	Ser	say	1.74
\$ 5		3149		GLa	Val		Fre 1150		3lu	Thr		Gln 1155		"Na	Als
50	37.2	Phe 3165	Leu	ae a	tys	i bêu	Ala 1165	Яìу	Arg	****	Pre	981 1170	loys	VAL	Va.i
55	Mis	75173	A) &	345	m)	801	Ast 17.80	Pho	Thi	ser	818	81a 1105	981	Lys	Aie
30	Ala	Cys 1190	Try	770	418	Aen	11e 1195	gt n	316	#10 a	Phe	61y 1200	110	Pro	Tyr
	Aen	Pro 1203	Ø1s	ser	33%	ŭ)y	Vs1 1210	Va.i	Ala	Ser	Mos	A88 1219	Lyt	Gå u	Lest
85	iys	tys 1230	1)e	214	Sty	G) n	Val 1225	Arg	Asr	oin	Ala	131u	His	1483	Dÿs

											71				
	The	Ala 1235	Val	ale	Net	Ala	Va1	Pile	Tle	His	Asp	Pise 1245	Lys	Arg	Lys
5	GLy	Giy 1290	22.6	919	at y	Tyr	Ser 1955	Ala	Sly	7i n	Ang	1260	Ile	Anc	130
10	11.4	Als 1265	Miss	Ang	Lie	(E) ri	THE 1270	Lys	WI.	Leny	nlu	Lys 1276	Gla	ale	Thr
15	Lys	118	Gin	Aes	Pisa	Arg	9al 1265	TYK	Tyr	Arg	hep	30r 1230	A29	Asip	980
20	274	Try. 1295	Був	dly	Pro	Alm	Lym 1300	žanu	Lens	žrp	Lys	Gly 1309	Olu	Ø1 y	Als
	¥a1	Val 1319	fie	Win.	Aug	Assi	Sey 1315	Asç	11e	Lys	Val	Val 1326	řeo	Arig	A2'9
25	ьув	A10 1935	Lys	110	Leu	Arg	Asp 1330	Гут	Gly	198	Gla	Met 1395	818	214	Asp
30	Anp	092 1360	Val	218	diy	Ang	91n 1345	Ang	Glu	λυδ	Arg	Ser 1950	Net	93 y	Gly
35	Lys	rip 1398	ser	Lys	G) y	Ser	114	Val	G17	Tro	Pro	910 1365	%)e	Arg	Olu
40	Azy	Met. 1370	AUG	Are)	Ala	990	Ala 1375	Ala	Ale	920	@1 y	Vál 1389	937	X.1 a	Val
	Ser	Gin 1388	Asp	tiesi	ARP	Lys	Bis 1390	Gly	ASA	ite	The	3399 Ser	Sex	Asn	Sle
45	Aso	Assp. 1450		Ses	Sys	Val	Trp 3489	Lenz	(Sia	Ala	ain	010 1418		Glu	Glu
50	Val	Gly 1419	Pag	Pro	Lay	Ang	980 8426	Gin	Val.	910	ten	Ang 1678	Pro	Met.	The
55	Tyr	Eye 1430	Gly	Ala	Pho	Assg	Les 1435	Ser	Ris	the	Len	bys 1840	Slu	Lys	Gly
80	Oly	Leu 1445	Asp	Gly	let:	rie	7yr 1450	G#1	Arq	Lye	Arg	@ln is59	91u	fle	Lev
	Anp	1460 Emm	Tep	Val	Tyr	Nim	7hr 1465	G) ri	dly	Tyr	Plac	Pro 1470	Avp	Tep	035
65	Asn	Tyr 1475	The	210	Sly	260	Gig 1480	Vs)	Arg	TYE	Sxo	1485	The	Ma	0.59

	72	
	Tep Cys Phe Lys Leu Val Pro Met Glo Pro Asp Glo Val Glo Lys 1490 1490	
5	Als The Giv Gly Sin Ann Ann See Less Inns Nid Prin 11e dyn Gin	
	1505 1515 1615	
10	His Sty Met Asp Asp Giu Giu Arm Gim Val Leu Lie Tip Lys She 1820 1830	
15	Amp Ser Arg Lev Alm Lord Lye His Amp Alm Glo Glu Lew Mis Pro 1515 1546	
20	Hit Pine Typ Lys Amp tys 1880	
25	*210 5 *211 3025 *212 DBA *213 BBY	
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	(coadamaga acaaggaagga matquagama tepangettom acatgarama aquentgraga	480
45	gelaagaago agcaggtgia cagoottgito lacoggotgg momlogagaa galomasaaso	349
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	tgenatangg tgaeritoga generitras arenastast populourge oggettogen	260
50	accutivade Brancharac chadrenam dacacobaco cordumnias elitableaco	725
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55	crimicaleds dedentable descellast dessenanci acsesseda assistant	840
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	angagetaru janteggere typernyade tretasyrda engadategt gogegacate	960
60	agacságort atthéasigt jintagjatt heriógsata accentisag attagiggen	1020
	ascrágotán gázagtacit vagráscang occatostát venecamena cagogyagán	1090
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5	990	ctga	999	cgac	cego	ga s	9909	guaa	c se	ceist	gob s	coe	acya	905	ve t ti	Agent.CE	1386
40	490	39c9	989	2632	7098	98 0	4300	3548	3 49	cyng	origi.	acas	egn. 8	0282	egte	grosag	1269
	*16	3450	100	1939	ogte	ge e	ecea	CBQ	90	2009	aga a	gag	SQt.	00A	9099	gaga ng	1500
10	393	decend.	t:29	grat	agger	ac c	gr <i>ā</i> r	es es s	3 99	ch te	ca.gg	gage	cge	ciós.	atc't	ecsati	3865
	gga	gcog	cca :	gest	canc.	et 9	acceg	tgeas	3 30	coga	cage	two	tgag	098	crent, cu	gtycag	1620
15	cag	caga	304	ator	gotg:	eg &	gode	toga	90	cesd	çaga	930	egge	366	ge v g	ecagte	1686
10	tigg	39C#	t ca	e qua de	geto	da g	gode	tog t	\$ 500	ggde	3:59	25.56	ysta	300	Septiments.	gastag	1940
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20	36#	agew	get s	ggag	caac.	\$ ×4	sget.	sogs.	day.	2840	sage.	SQ 83	ecat:	380 ·	24.63	otycag	1866
	1.99	gace	499	3333	2990	23 6	6262	ccam	C 348:	087.6	caca	god	egati	098	9939	agodag	1926
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30																	
35	4.40	0>	6														
	Mat.	AUG	Val	Mes	G16 5	236	MIN	Arg	Aen	Cya 16	Gin	His.	inu	\$60	A29 15	Trp	
10	3)3	134	Phint:	71e	Letu	oly	Mest	:le	rle 25	Lin	cys	Sal	THY	ala 30	day.	Asn	
45	Leu	Tep	Va1	me	Val	tyr	Tyr	Gly 40	Ye)	Fro	983	Тер	Acry 45	Aep	Als	(33 to	
50	The	The So	Loro	Ptie	ōya	Ala	343°	Asp	Ain	tya	Als	60 173	365	Thr	G) (1	190	
	Min 65	Ass	Val	Trp	Ala	The	line	818	Cye	Vel	920 75	27.2	Asp	Pro	Asti	Pro 80	
55	Gle	Gio	Tie	Fro	Les P5	Aep	Aen	Val	Thi	61 u 96	Glu	Pha	ASC!	Met.	5232 8%	Eys	
50	ASA	Nat.	Met	Val.	Ang	Mir.	Met	Mass	014 168	Ang	Ils	1)6	803	110	gap	Ye's.	
35	GLR	Shr	Lero 179	Lys	FIC	Cys	val.	31n 320	Len	The	Sic	િલ્લ	Cys 135	va;	Thr	u#ti	
	Asn	Cys	530.5	han	ALS	Arg	Val	Ask	Ala	Thi	Pha	Asn	Ser	The	Gla	Ass	

		130					1.36					548				
5	A19 145	Gla	Gly	Net	Lys	Asa 155		Ser	Pin	Aen	Mas 155		321	61%	Less	#19 169
10	Asp	rya	Lys	Dln.	01e 168		žyn	Ser	Less	9he 130	Tyr	årg	Lega		11 <i>m</i>	Ġħo
	Lys	Ita	aen	der 188	der	App	San	Asn	391 185		Tyr	Arg	1/94	Ve 1 150		Cys
15	naA	thr	Ser 193		Tie	Chr	ove	A) a 200	dys	Paro	Ŀķs	Vs1	7hr 205	Phe	Olu	Pro
30	116	Pro 219		His	278	Cys	335 335		X14	Qly	She	Ala 220	Tie	Leu	Lys	Sha
25	Asn 225	Asp	The	o)n	Pine	A.o.s. 210	aly	Tue	dly	Pro	Cya 235	bys	Asn	983	Ser	7hr 246
36	Val	Gln	Cye	The	His	017	The	Lys	Pro	9al 25d	Val	Sar	That	Gin	lera 259	Lec
	Løu	Asn	Gi y	Sex 260	14FU	Ala	gg v	Arg	010 265	Va:	Avg	110	803	Ser 276	919	Asn
35	lle	Ala	Asn 275		Alx	Lya	Aan	11e 286		Yal	Cin		Ala 185	Ser	Fra	Val
40	iye	114	Asn	tys	210	Arg	980 290		Astr	ARR	Thr	819 300	Lys	ser	tyr	Arg
45	119 305	Giy	Pro	gly	afo	The 31.0		7уе	Ala	The	Asp 313	Ile	Val	Gly	Asy	310 320
50	Arg	Gla	Ala	Bis	0ys 325	ARA	VAl	Sec	ALL	Thi 330	880	Tip	Astr	Asu	1748 336	Letu
	Arg	Leo	147	Ala 546		G.n	660	Arg	545 545	375	270	Ser	Aen	350	The	116
55	Sle	Plu	Thr 355	Assn	Sect	Sec	Gly	G1y	Assp	Leu	Çla	Tie	The Sec	The	Hix	Ser
60	FTY	A85	CAS	dly	Gly	Glv	95e 395	PNe	Tyx	Cys	286	Thr 340	Sex	sty	100	Fite
65	305		Stori	Tip	The	10.7	Asc	Asit	Max	ola	91c	Serr	Assis	Aep	25.0	261 405
	Aun	Gly	SPA	ile.	345	Leo	Pro	Cyla	Arg	130	Light	ÇÎn	110	Ile	Arg	Mer

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5	Tep	Ole				Gia	Ais	Stell.	Tyr 425	Als	63.43	Fro	110	@10 430	gly	9al
10	7. Q	Arg			Sex	Aso				Leu	Tie				Amp	Oly
	919			Ass	Ser	Ala			The	Phs	Arrg			Gly	Gly	Asg
15	710	Arg	Aeg	Asn	2.2.25	Arg	Ser	Olsa	Low	Tyr	175	Tyr	Lys	Va:	Vell	14s
20	110	630	140	Teo	@).y 485	wa;	Rim	900	The	Arg 400	A) a	ty's	Axy	åxş	Val 498	Val
25	035	203	my	Lys	Arg	878	Va.	3) Å			s)a	v.s.i	Price	540 520	Gly	Pae
30	Line				Gly	Sec	The			Ala	Ala	Ser	11e 625	The	Lift	The
	Va).	016 500	Ala	Arg	Cin	Leg u	149u 535	Ser	317	11e	Va)	Gin Sed	GIn	Gla	961	Asu
35	54.5	Leu	Arg	Ala	ile	Clu 55.8	Ala	Gla	WI n	qin.	£60 859	Linu	Lys	Leu	Thr	Val
40	TXp	Φîγ	314	leye	Gin S&S	Leu	Gln	Ala	Arg	Va.1	Leo	ADB	Val	016	Art 575	żyż
45	Leu	Ar9	ALC	Gla 685	Oln	Leu	ten	GCy	11e	Trp	Gly	Cys	Ser	61y 180	Lys	Les
50	110	CAs			Aen	Va)	200	555 555	APD	Ser	Ser				Lys	Ser
	Tyr	825 610	Aug	110	Trp	Ola	App. 615	Mark	West of the last o	Try	Leo	Gla 520	Tep	Asp	Lyp	15 k (2
55			Aon	242	Dix			110	*ye				Glu	Gla		Gla 849
60	ĀRS	ala	aln	6) vi			ayn.	លាក				nía	Lani	వజ్ఞు	160	
65	Ala	Aes	1.eu	Top 660	ăe6	Tro	Phe	Asp	71e 663	She's	Liye	TIP	Lefte	713 670	Tex	Tie
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55	ggcacrgsag	ygaetgygac	agagastgag	acagagatet	tragacocog	aggaggagat	3440
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45		Aur	lle	4,332	Cly		Len 455		The	Arg	Asp	01y 460	diy	Thr	Chu	oi:
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<213s Mycobetterium tuperculosis

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-2135 Plagmodium falcinsmum

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Not Arg Lyn Leu Aim Lie Leu Ser Val. Ser der Phe Reu Pee val. 10 43 55

Glu Ala Leu Ahe Glo Glu Lyr Glo Cys Tyr Gly Ber Ser Ser Ann Thr 29 . We have also Leu Ahe Syr Ann Ala Cly Thr has Leu Tyr

Ass the less the wet as ye tyr the the the the tre tyr ser to

Les Lys Dys San Ser Arg Ser bed Cly Gla Asn Asp Asp Gly Asn Asn

	65					70					75					80
5	346	Aeti	Sty	Asp	8.88 88	sty	Arg	904	Bly	Lys 96	Asp	914	Asp	Lys	A.899 95	Asp
10	60'9	Axes	ÅRT	She Loc	AND		314	Lys	Leu 109	Bitte	Lyw	Pro		85a 210		Lyi
	Leu	Lys	Gln 115		Ala	Asp		880 126		Asp	Pro	Aso	Ala 125		Pro	Asr
15	Va1	88p		Asso	N) a	Sen	970 178	Aero	Val	Āsp	Pro	Aen 190	Ala	āso	P26	Aer
20	vai 348		Pro	Ann	4.6.4	Aun. 150	Pro	Aun	27,50		Pro 166	Aun	s la	ភ័ន្តខា		Sar Sec
25	Ale	Aso	Pro	084	Ala 168	Asn	PYO	San	Mia	Asn	800	Asp	Ala	Asn	\$20 175	
30	Ala	Ann	Pro	Ann 186		Ann	Pro	Aun	Ain 185		מוזיל	Ann	Ain	Asn 190		Aar
	ya)	çaA	9200 2.95		Ala	Aso	9ro	Asn 205		Aan	¥20		Ala 109		\$210	Asr
35	Ala	Ass 219	260	Asn	Als	Asn	219		Ala	Ass	Pep	Aen 220		Asa	\$50	Ass
40	818 225	880	FXTO	888		A60 230		848	818	A&B	200 235	380	Ala	ARC	PXO	A60 240
45	Ale	Asn	Fro		Sin 245	Ann	620	Apri	Als	Aso 250	Pro	Ass	7.1 to	Aso	Fro 295	
50	838	8.85		8#6 260	8.18	8.9%	946	805	818 265		P2/5	Ass	Lys	A80 279	ABO	GG Y
	aly	Ago	01y 278	din	lity	His	Asn	Met.	180	Aon	Aap		A42 285		Aun	Val
55	Asp	Q1u 290	Aesn	Ala	Aati	Xla	Asn 298		Alæ	VAI	Lym	Asn 308	Ann	Asn	Aan	60.
60	(i) u 309		See			Ris	130	Lyn	ai n		200		Lya	238	din.	AX2 320
65	Ser	Lettera.	Sex	This	016 335	rry	961	\$ 800	Сув	Sex 336	Val	The	Cys	Gly	Asii. 335	(F)
	Tle	dîn	861	Arg	Me	Lys	Fro	GΊγ	Ser	A18	Ass	Lye	\$-20	Lys	Asp	or in

34% 345 385 Den Asp Tyr Ala Asn Asp The Glu Lys Lys He Cys Lys Met Glu Lys Cys Ser Ser Val She Asm Val Val Asm Ser Ain Ilm Gly Leu 375 10 <2385 13 c2319 1225 AME CCIUS 15 22224 Clasmodium falciparum WANGS 17 atgauggeur cogatoutsa sychastron haigumaalo caanogemaa solonaatgim 60 20 saturtastu osasperas rerastiro Sapresaro Dissturtes indesenció 3.28 astresasty reservings cycansomic antyraanth otmosporms tecamatyrs 180 autoresako osasecessa tarasaceoa satgoasace reastgosas tectastass 340 25 ancastramo quastrosco apotrecast successors accomance asstatevat 300 gaymangotik kigonikong igotyrosak katakisata bogsagawo sagogateky 165 30 cacatasaag astactesaa caasatacaa asttocoutt basetgsatt grootcatgu active depresent of the second 680 seegacges; tagatteign sestgetelt gammamama frigteamht ggammangt 640 35 todagtgrgs ttaatgregt aaaragtrom ataggartam ggootgtged geacatggag 800 868 daratoscas, coggations aggardency ologogyttas aggregogytt titotigity 40 evesysator toscsetare oragequete garacetegt egarcinist executivits gggggandac ongigigist ngganasaan tegnagteor caaccidoss thactdaces 225 accoderate rerespitta tectoritat ractoritat atalacomo iticatosta 840 45 trectores protected; suspendent theiraries trentotess thatessest 999 etaingonig intercence Westernage coesciences constangue endangeses 253 50 acolgouches evoctyetes aggesablet algeblocch dengingeng tacasables 3525 anggatggas stignanning istroporath cosmosioni gggotitogo assatiscora 1050 topgagtogg beroagheeg teleforing otcagnical cagigodate igicoagtog 1243 55 rtegraggge triotecrae sgittiggelt teagetatat gyargatgig grattgiggg 1090 creaginings adagosings gagknoonis atarogengs tarmastics distining new 3266 60 toggstataon thian x2503 14 +221 × 426 66 4232\ PRO .213> Plasmodium falciparum 4405× 14

	### E	Sect	Ala		Aep S	920	840	Ala	Asc	Pro 10	San	5) 4	Axn	Pro	Apn IS	818
5	Asn	250	Ass	A) a	Asın	Pro	Äsn	Ale	Asn 25	Pro	Ann	Ala	Asn	\$200 30	Asn	Ale
10	Assa	Fro	A800 35	Ala	Asn	***	X (80)	Ala es	Ann	Pro	Zan	Ala	Asn 45	\$20	Asm	Als
15	Asp	6.0 6.0	Ass	Ain	Asn	Fro	Asn SS	Ale	Asses	Pro	Ann	Als 60	Asn	820	Asm	Ala
20	Ada 65	250	Ass	Aia	Aen	200	Asn	ATA	Ass	Pro	A#8 75	Ala	Aen	\$16.0		1.91 80
	Asu	Asa	nia	Wiy	Asn 85	Gly	win	Wiy	His	A86 90	Mat	Evo	Axr	Asp	240. 95.	Ass
25	Arg	Ase	Vel	Asp 388		Aen	Ala	Asn	Ale 385		Ser	3.) a	Val	Lys 110		Ass
30	688	386	33u 135	53 ti	Pro	Ser	Asp.	130		List	Lys	Ola	Tyr 125	\$40 c	A-30	legs
35		130 130		Sex	i.eu	Ser	Thr 135		rep	Ser		Ops 148		val.	Tir	Cys
40	019 148		Gly	Tle	016	Val 299		Tie	Lys	Pro	Gly 188	848	Ala	Aso	Liya	161
	Cys	Asp	G3 u	les	Asp 165	23.0	Ala	సేజర	Asp	11e 179	Glu	tyn	byx	ile	Cyn 175	
45	Met.	gtu	Uys	Cys 185	Ser	Çer	Val	25 a	Asn 185	751	Vsl	Asn	Ser	Set 195	Ile	Q1 ₃
50	lieu	673	770 193		Thr	Ass	Mes	240	Asse	Ile	The	Bern	01y 205	Phie	Lara	G15
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	City	GRY	Sex	200	743 248	Cys	Leis	Sty	sin	A#8. 250	Ser	G) n	Ser	880	The 285	60)
65	Asn	Ris	Secr	250 260	Thr	Ser	Sys	222	910 250	216	Cys	PTS	oly	75T 270		arr

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5	1.06	11a 290	Fha	Less	5 eu	Val	Lieus 295	leu	asp	Tyr	Gla	388 618	9000	Leru	Pro	VX.I	
10	Cys 365	êzo	Les	114	Pro	Gly 310	aer	TAR	TRE	The	Aan 335	TRY	019	PRO	Cys	1-ye 320	
15	Thr	Che	ane	Tar	PY6 325	sia	n fat	6) y	Agen	Ser	Met	\$700	Pro	Ser	Cys 336	Cys	
20	Cys '	242	Lye	Pro 340	The	Asp	(i) y	äso	Oya 345	TES	Cya	Tie	Pro	350	Pro	for.	
	ser '	rry.	Ala 365	Phe	Ala	ty s	Tyr	260 360	rep	Gle	Trp	Ala	Ser 365	29.1	Arg	The	
25	Sec '	Trp	Leu	Ser	Lou	Lev	7a1 375	Pro	Floe	Ya:	dia	Trp	File	Val.	61 y	Leu	
30	Ser 365	\$25	Thr	Val	Txp	1.00 1.90	Sex	ALR	210	Trp	Met 388	Merc	Tep	ryr	Typ	Giy 400	
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25	coglenctas	agatgggcta	egagerteat	roggacaagt	dhanadnace	godystagty	3040	
	поделервия	aggastoring	gacogtmant	gacatroaga	auerag; egg	cappet base	1596	
30	tgggdoteco	agacteacod	aggoattaag	gcoogscage	ttogoaaget	accgagggga	1560	
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	gegaategeg	anaogaagct	aggovagggog	ggatacgtgs	ctastagggg	оедоскавад	2100	
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	aggegepagg	statterige teig	togate taccahacec	egggtest tonggestgg	2760
	Cagaaltaca	ccenaggen agac	gegege tearcacanga	otitogggig glentacaea	2820
5	ctagodedag	togaschoda caso	gtowae gapqotbala	agagegagas nabunciens	2880
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10	thogastots	gacitiquest comm	cacqta gcacgogago	tgoatobaga atatitomay	3866
	aagegeegee	caacaggcgc cage	groadt gractbageg	goggagaact agatogatgg	3060
	gasaagatac	geotaegede 8993	gucasy asgragusca	agehtaagea cattgugigg	3530
15	gestavagog	wastegageg atte	googte metocogyco	tgcttgagac gagtgaaggc	3385
	tgtaggcame	tucngagaca gata	concer apertacage	ctypengage @gegattagt	3246
20	agereceasa	stacogrege gace	cuctae tgogithoaud	bacqastogs ascamages	3300
	actasagagg	decit gatas autt	gaggag gaacagaana	agrosamame quaggereag	3366
25	caggeogoey	ongenanngg goed	aşısan maggiglini	s asserbease	3433
30	<pre><210 * 16 <211 * 113 <212 * PPT <113 * 819</pre>				
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35	Met Val 11	e Val Glo Asn Il 5	e Gin Gly Gin Met	Val Ala Gin Ala 31e 13	
40	Sor Pro Ar	g The Low Ann Al 20	a Trp Val Lye Val 35	Val Glo Glo byw Ale 30	
	Phe Ser Px 35		d Mes Pae Sav Ala 40	hec ser Gib Giy Als 45	
45	The Pre Gi	n Asp let Aso Th 95		Val Gly Cly Mis Sin	
50	Ala Ala Me 66	t Öln Met Leu Ly 76	s Clu Thr Ile Asm 75	Olu Olu Ala Ala Olu 80	
55	Trp App Ar	y val His Pro VA 95	i sta als dly Pro 16	lie wie Pro Cly Glo	
60	Met Ang II	u Pro Ary My Se 198	r Asp the Ale Sty 105	the The See The Law 110	
	The classic states of the contract of the cont		C Thr 506 ADS Pro 120	Pro lie Pro Val Cly	
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	Met 345		der	950	The	Sec 150		Leu	Авр	lle	Arg 193		Gly	Pre		61a 360
5	210	2700	819	seg	Tyr 165	Val	Asp	Arg	Phe	TYE	Lys	The	besi	arg	Ala 175	-G) u
10	Gla	Ala	802	01n	314	Vai	Lys	Azri	Trp 185		The	Olu		Leo 190		Va)
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20	.63a	A) 5 210		Lena	Glu	935	Met. 238		Tire	Ala		Gla 220		Val.	Gίγ	Gly
	226	gly	His	Lynn	Ala	939 819		1,90	Sis		gly 335		Tie	SAT	Pro	11e
25	Olu	The	Val	Ser	V63	bys	Letu	Lve	Pro	Gly	Met	Asp	Gly	P30	Dys 255	Val
30	Lys	Oln	Ткр	Pxo 268	Lev	The	Slu	Sin	1.998 265		Lys	Ala	leso	Vel. 200	Gi sa	154
35	Cys	Thr	#19 #29	Ne z	Siu	2,78	Glu	Gly 280	lys:	Tie	Ser	5/y s	110 285	Gly	PEO	Q) a
40	Ana	P200		ASD	Thy	220	V#1 295		A16	114	Lys	144 140	Lys	Asp	Ser	the
	Tyn 398	Ten	Arg	Lye	\$49x:	val 115	Asp	Fbs.	Arry	0) ម	1.001	Fan	Toy is	Mrg	Tar	330
45	Azp	phe	Trys	0) u	Val 325	Gia	Lev	Bly	116	Pro 330		Pro	Ale	Gly	586 336	
50	Lys	sye	ly s	Sex 345	VAR	Thr	Val	ies	A90	Vai	G1 y	Aap	838	198 350	Phh	Ger
55	983	Fro	355	Asp	Ola	Asp	Stie	Arg 740	Lys	Tyr	Thr	Ala	256 355	4417	1) e	FFO
60	Ser	110	Aan	Ash	Ole	783	9x6 375		lle	Arg	TYX	Gln 386		Ass	va:	Lev
	P#0	Gin	dly	Trp	Lys	019 390	Ser	Pro	Alk	lie	etie 395	01n	Ser	Ċys	Kec	13sr 408
85	Lys	fle	Leu	Glu	92°0 405	Phe	Arg	tys		Asn 418		Asp	tie	Val	11e 416	

	9 1															
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20	iøs:	Pro	6Jn	Lys	A85 495	808	Typ	Inr	Val	Ass 496		116	Glu	Lys	180 495	Va.
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25	Gin	Len	Cys 915		Leu	ben		Giy 920	Mar	Lys	Ala		7hr 525		Val	ile.
30	210	16u 510		GID	Olu	XIX	01u 535	inu	737 to	Les	Ala	930 566		Arg	910	234
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40	130	Als	Gie	3) 0	61n 965		din	613.	Gln	91y 578	ene.	Trp	The	3.25	9in 575	478
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45	Arg	Sty.	828 595	Ris	Tt.r	Aes	Aep	Vai 600		G) a	Leu		G1w 585	Ala	Val	G36
50	toys	11* 619		The	31.5	Sec	110		214	Trp	en.y	£98 €20	382	Pro	Lyn	Pag
55	628 628		Fro	110		542 540		TBY.	Tup	©in	Thr 635	Trp	THO	Thr	sto	TYX -645
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	l≫ű	vai		14u 460		278	33%	Orie	614 665	bys	Glu	Fro	ile	Va3 67#	giy	Ala
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	Lye		Gly	375	941	Thr	A80	arg	aly	Arg	Gla	Lys 200	Ves 1	Vis 1	The	240
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15	Ale	lieft	63.5	11 <i>e</i> 740	110	QI n	ASa	sin	910 745	Aep	©In	Set	GEO	Sex VS0	63th	Le
20	Yal	Asn	GIR 75%		Ele	G1a	Cin	linu 760		Lys	£ys	152 ia	Lyn		Tyr	Ž:m
	Ala	Tep 776	lev	Pro	Ala	Nis	Lys 775	GH y	118	Gly	GD 9	Asn 780	GUI	Gla	Val	Asp
25	196	Leu	Val	Sec	Ala	330	110	Azg	bys	Vai	755	Ala	mes	Gly	dly	5y6
30	3,525	Ser	Lys	Sec	Set 805	Val	Val	SIY	Trp	Pro 819	Rhe	Val.	Arg	G2 o	Arg 815	Merc
35	Ary	Arg	Ala	Glu 823	Pro	Ala	Ala	Asp	01y 825	843	317	Ala	Ala	8er 836	Arg	Asi
40	Leu	81 s	Lys 836	Sis	01 y	Ala	lie	The 240		Ber	Asn	Thr	A1 a	0.1 x	Thr	Ast
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45	Pro 069	981	Abir	Pro	QIa	Vai 875	Pro	Leo	Ang	fro	Met #76	Wer	Tyr	Lyn	Ala	A14
50	Val	Asp	Leu	Seg	819 885	Phe	Lehi	Lys	Glu	try 8 8 9 6	άŝγ	diy	ten	G) u	Sly 895	5.61
55	134	His	Ser	015 900	åxų	8.03	\$3.6	Asp	11e 905	Tera	Asp	Seu	Tre	11e 910	Tyr	31.5 s
60	The		0)y 919		Pto	Pro	Aap	77p 920	016	Aen	tys		Pro 325	Gly	Pris	Giy
		A19	3/18	800	Less	The	She 935		řep	Cys	Tyr	Lys	limi	Val	Pro	va.
65	01 to 94 S	\$110	Asg	Lyn	Val	619 850	alu	67.8	Net	Lys	Gly 995	918	Asc	Tha	991	564

	Leu	Ris	bro	Val	Ser 965	le a	Bis	Oly M		ap A	sç F	ro Gl	u Ar	9 02	
5	les u	Glu	тар	A29 980	\$1.0	Анр	Set .		el. A	la P	tje X	is Ni	9 VA		8.8
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All references referred to in this application, including patent and petent applications, are incorporated herein by reference to the fullest extent possible.

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Throughout the specification and the claims which follow, unless the context requires otherwise, the word 'comprise', and variations such as 'comprises' and 'comprising', will be understood to imply the inclusion of a stated integer, step, group of integers or group of steps but not to the exclusion of any other integer, step, group of integers or group of steps.

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The application of which this description and claims forms part may be used as a basis for priority in respect of any subsequent application. The claims of such subsequent application may be directed to any feature or composition of features described herein. They may take the form of product, composition, process, or use claims and may include, by way of example and without limitation, the following claims:

Claims

- 1. A method of raising an immune response against a pathogen which comprises administering (i) one or more first immunogenic polypeptides derived from said pathogen; (ii) one or more adenoviral vectors comprising one or more heterologous polypucteotides encoding one or more second immunogenic polypeptides derived from said pathogen; and (iii) an adjuvant; wherein the one or more first immunogenic polypeptides, the one or more adenoviral vectors and the adjuvant are administered concomitantly.
- 2. A method of raising an immune response against a pathogen which comprises administering (i)) one or more first immunogenic polypeptides derived from said pathogen coformulated with an adjuvant, and (ii) one or more adenoviral vectors comprising one or more heterologous polynucleotides encoding one or more second immunogenic polypeptides derived from said pathogen; wherein one or more immunogenic polypeptides and adjuvant, and one or more adenoviral vectors are administered concomitantly.
- 15 3 A method of stimulating the production of pathogen-specific CD4+ and/or CD8+ T-ceils and/or antibodies in mammals which comprises administering to said mammal (i) one or more first immunogenic polypeptides derived from a pathogen; (ii) one or more adenoviral vectors comprising one or more heterologous polypucteotides encoding one or more seen in munogenic polypeptides derived from said pathogen; and (iii) an adjuvant; wherein the one or more first immunogenic polypeptides the one or more adenoviral vectors and the adjuvant are administered concomitantly, for example by administering an immunologically effective amount of an aforessaid composition.
 - 4. A method of raising an immune response against a pathogen which consists of (a) administering (i) one or more first immunogenic polypeptides derived from said pathogen; (ii) one or more adenoviral vectors comprising one or more heterologous polynucleotides encoding one or more second immunogenic polypeptides derived from said pathogen; and (iii) an adjuvant, wherein the one or more immunogenic polypeptide, the one or more adenoviral vector and the adjuvant are administered concomitantly; and (b) optionally repeating the steps of (a).
- 5. A method of raising an immune response against a pathogen which comprises administering (i) one or more first immunogenic polypeptides derived from said pathogen; (ii) one or more adenoviral vectors comprising one or more heterologous polynuclectides encoding one or more second immunogenic polypeptides derived from said pathogen; and (iii) an adjuvant: wherein the one or more first immunogenic polypeptides, the one or more adenoviral vectors and the adjuvant are administered concomitantly; and wherein the method does not involve administering any priming dose of immunogenic polypeptide or polynucleotide encoding immunogenic polypeptide.

- A method according to any one of claims 1 to 5 wherein one or more immunogenic polypeotides, one or more adenoviral vectors and an aditivent are co-formulated.
- A method according to any one of claims 1 to 6 wherein production of pathogen specific CD4+ T-cells and CD6+ T-cells and entibodies is stimulated.
- 5 8. A vaccine composition comprising (i) one or more first immunogenic polypeptides derived from a pathogen; (ii) one or more adenoviral vectors comprising one or more heterologous polynucleoide encoding one or more second immunogenic polypeptides derived from said pathogen; and (iii) an adiuvant.
- A method or vaccine composition according to any one of claims 1 to 8 wherein one or
 more of said one or more first immunogenic polypeptides is substantially the same as one or
 more of said one or more second immunopenic polypeptides.
- 10. A method or vaccine composition according to any one of claims 1 to 8 wherein one or more of said one or more first immunogenic polypeptides contains at least one antigen which is substantially the same as an antigen contained in one or more of said one or more second immunocenic polypeptides.
 - A method or vaccine composition according to any one of claims 1 to 10 wherein one or more the first immunocenic polypectides composes at least one T pall spitope.
 - A method or vaccine composition according to any one of claims 1 to 11 wherein the one
 or more first immuniperic polybeolide comprises at least one B cell epitope.
- 20 13. A method or vaccine composition according to any one of claims 1 to 12 wherein one or more of said one or more first immunogenic polypeptides and one or more of said one or more second immunogenic polypeptides where one or more identical B-cell and/or T-cell epilopes.
 - 14. A method or vaccine composition according to any one of claims 1 to 8 wherein none of the one or more of said one or more first immunogenic polypeptides is substantially the same as
- 25 or contains any antigen in common with one or more of said one or more second immunogenic polypeptides.
 - 15. A method or vaccine composition according to any one of daims 1 to 14 wherein one or more of the adenoviral vectors is derived from a human adenovirus.
 - A method or vaccine composition according to claim 15 wherein the human adenovirus servivpe is selected from Ad1, Ad2, Ad4, Ad6, Ad6, Ad11, Ad 24, Ad34 and Ad35.
 - 17. A method or vaccine composition according to any one of claims 1 to 14 wherein one or more of the adenoviral vectors is derived from a non-human primate adenovirus.
- A method or vaccine composition according to claim 17 wherein the non-human primate adenovirus serotype is selected from chimparizee adenovirus serotypes Pan6, Pan6, Pan7 and
 Pan8.
 - A method or vaccine composition according to any one of claims 1 to 18 wherein the pathogen is HIV.

- 20. A method or vaccine composition according to claim 19 wherein the immunogenic polypeptides contain HIV derived antigens which are selected from Env. Naf. Gag, and Pol and immunogenic derivatives thereof and immunogenic fragments thereof.
- A method or vaccine composition according to claim 20 wherein a first immunogenic polypestide is p24-RY-Nef-p17.
 - A method or vaccine composition according to claim 20 or claim 21 wherein a second immunocenic polyceptide is Gac-RT-Nef.
 - A method or vaccine composition according to any one of claims 1 to 18 wherein the pathogen is Plasmodium falciparum and/or Plasmodium vivax.
- 10 24. A method or vaccine composition according to claim 23 wherein the immunogenic polypeptides contain antigens derived from Plasmodium falciparum and/or Plasmodium vivax which are selected from circumsporozoite (CS) protein, MSP-1, MSP-3, AMA-1, LSA-1, LSA-3 and immunogenic derivatives thereof or immunogenic fragments thereof.
- A method or vaccine composition according to claim 24 wherein a/the immunogenic
 polypeotide is the hybrid protein RTS.
 - A method or vaccine composition according to claim 25 wherein RTS is presented in the form of a mixed particle known as RTS.S.
 - 27. A method or vaccine composition according to any one of claims 24 to 26 wherein arthe immunispenic polypeptide encoded by a polyhucleotide is the CS protein from Plasmodium falciparum or immunogenic fragment thereof.
 - 28 A method or vaccine composition according to any one of claims 1 to18 wherein the pathogen is. Mycobacterium tuberculosis.
 - 29. A method or vaccine composition according to any one of claims 1 to 28 wherein the adjuvant comprises a preferential stimulator of Th1 responses.
- A method or vaccine composition according to claim 29 wherein the adjuvant comprises.
 QS21 and/or 3D-MPt, and/or CpG.
 - A method or vaccine composition according to claim 30 wherein the adjuvant comprises QS21 and 3D-MPL.
- A method or vaccine composition according to any one of claims 1 to 31 wherein the
 adjuvant contains an oil-in-water emulsion.
 - 33. A method or vaccine composition according to any one of claims 1 to 31 wherein the adjuvant contains liposomes.
- A method of stimulating an immune response in a mammal which comprises administering to a subject an immunologically effective amount of a vaccine composition
 according to any one of claims 8 to 35.
 - Use of a vaccine composition according to any one of claim 8 to 33 in the manufacture
 of a medicament for stimulating an immune response in a mammal.

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- 36. A vaccine composition according to any one of claims 8 to 33 for use in stimulating an immune response in a maintrial.
- 37. A kit comprising (i) one or more first immunogenic polypeptides derived from a pathogen. (ii) one or more adenoviral vectors comprising one or more haterologous polynucleotides encoding one or more second immunogenic polypeptides derived from said pathogen; and (iii) an adjuvant.
- 38. A kit comprising (i) one or more first immunogenic polypeptides derived from a pathogen and an adjuvant; and (ii) one or more second adenoviral vectors comprising one or more heterologous polynucleotides encoding one or more immunogenic polypeptides derived from said pathogen.
- 39. A method, or vaccine, or kit, or use according to any preceding claim wherein the first immunogenic polypeptide comprises p24-RT-Net-p17, the adjuvant comprises 3D-MPL and Q821 in a liposome such as adjuvant B heroin and the adenoviral vector comprises a chimpanizee adenovirus serolype Pan7 vector comprising a polynucleotide encoding the immunogenic polypeptide Gaq-RT-Net, optionally codon optimised.
- 40 A method, or vaccine, or kit, or use according to any preceding plain wherein one, or two, or all of the polypeptide, adenoviral vector and adjuvant components are combined with a pharmaceutically acceptable excipient.

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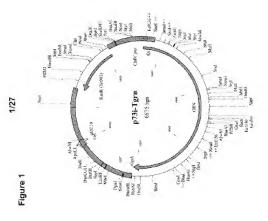
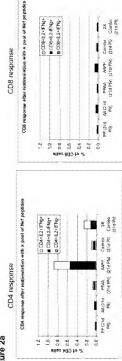


Figure 2a



CCD8-82-FNg+ BCXN-E2+KNg-

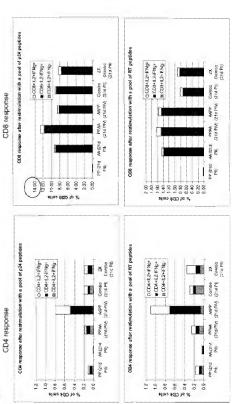
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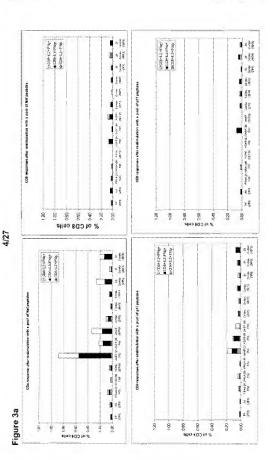
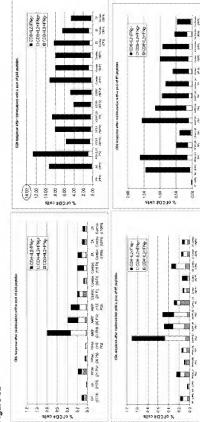
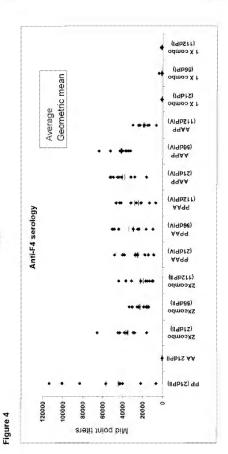


Figure 3b





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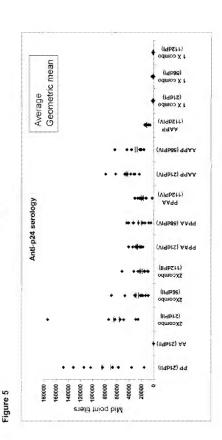


Figure 6

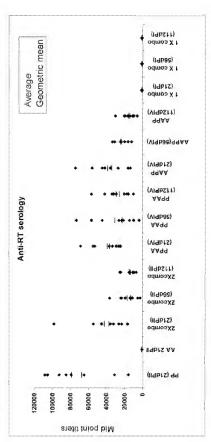
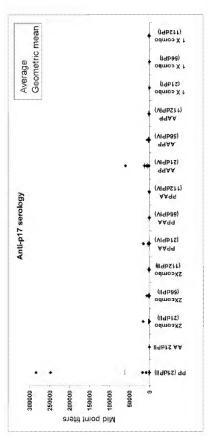


Figure 7





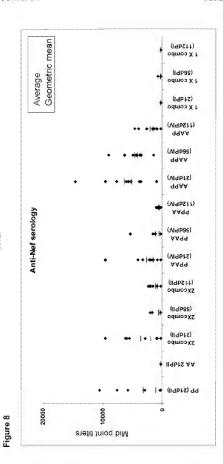
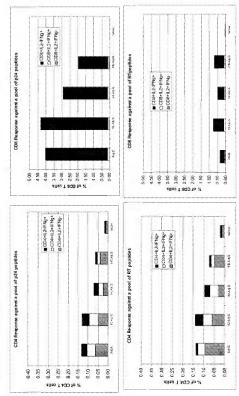


Figure 9



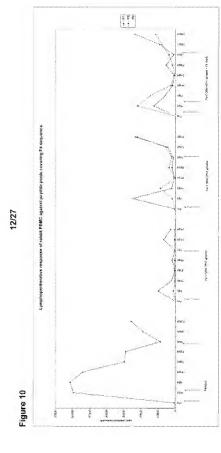


Figure 11

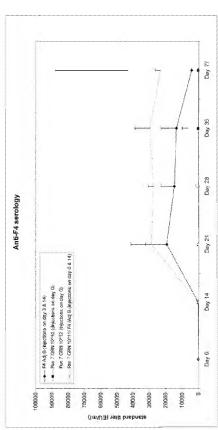
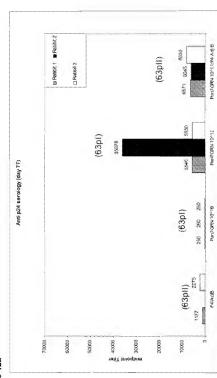


Figure 12a



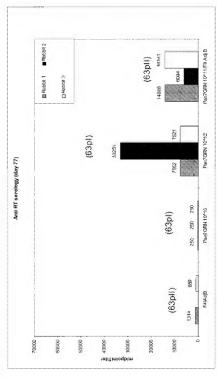


Figure 12b

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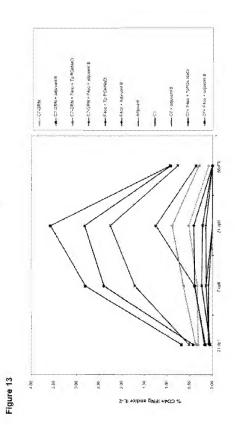


Figure 14

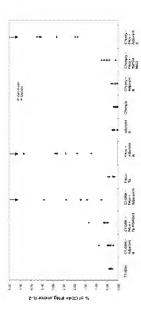
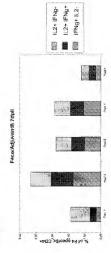
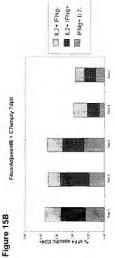


Figure 15A





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Figure 15C

Figure 16

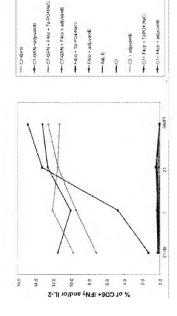


Figure 17A

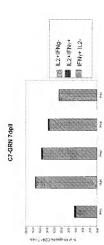
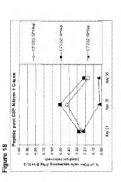


Figure 17B





Figure 17 C



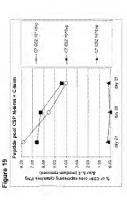
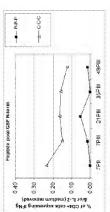
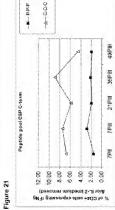
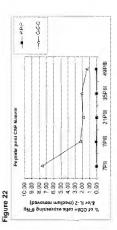


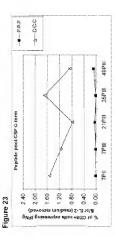
Figure 20

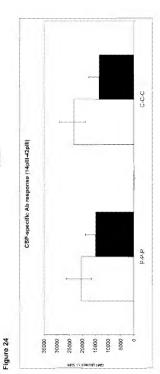












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Irion, Andrea

Faxc (#21-70) 340-3016

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